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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,169	04/27/2005	Andrew David Bacon	Q85454	9237

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,169	BACON ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,16,25,26,28-30 and 32-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,16,25,26,28-30 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed 12-30-08 has been entered. Claims 13 and 29 have been amended. Claims 27 and 31 have been canceled. Claims 32-35 have been added. Claims 13, 16, 25, 26, 28-30 and 32-35 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 13, 16, 25, 26, 28, 32, 34 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants' amendment filed 12-30-08 necessitates this new ground of rejection.

The phrase "the antigenic protein and the assistor protein are associated with the same liposome" in claim 13 is vague and renders the claim indefinite. It appears that the liposomes are associated with nucleic acid and assistor protein and the nucleic acid encodes an antigenic protein. It is understood that the antigenic protein has NOT been expressed by the nucleic acid in the liposomes. It is unclear how the antigenic protein, which is not expressed yet, and the assistor protein are associated with the same liposome. Claims 16, 25, 26, 28, 32 and 34 depend from claim 13 but fail to clarify the indefiniteness.

The term "and/or" in claims 34 and 35 is vague and renders the claims indefinite. It is unclear what is intended. It is unclear whether the term "and/or" is intended for phosphatidyl ethanolamine and phosphatidyl serine or for phosphatidyl choline, phosphatidyl ethanolamine

and phosphatidyl serine. Changing the term "and/or" to "...or...or both" and clarifying what is intended would be remedial.

The phrase "the phospholipids comprise phosphatidyl choline, phosphatidyl ethanolamine and/or phosphatidyl serine" in claims 34 and 35 is vague and renders the claims indefinite. The term "comprise" is an open language which means there are other phospholipids or unknown components are intended in the claims. It is unclear what other phospholipids or components are intended in the claims.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 13, 16, 25, 26, 28-30 and 32-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants' amendment filed 12-30-08 necessitates this new ground of rejection.

The phrase "liposomes are not polymerized" in claims 13 and 29 is considered new matter. The specification fails to explicitly or implicitly disclose that the liposomes are NOT polymerized. Applicants argue that although there is no in haec verba support for the phrase "liposomes are not polymerized", however, it is inherent in the specification because all of the

liposomal compositions described generically and exemplified lack a polymerization step (amendment, p. 5). This is not found persuasive because the specification is silent or vague regarding whether the liposomes are polymerized or not. The liposomes can be monomer or polymerized and it is NOT inherent that the liposome prepared in the instant invention is NOT polymerized. This is different from the cited Kennecott Corp v. Kyocera Int'l, Inc., where "equiaxed" microstructures are inherent because the preparation of the same material was described. Here the prepared liposome could be monomer or polymerized and the specification is silent or vague regarding whether the liposomes are polymerized or not. The amended claims require the liposomes are NOT polymerized, however, the specification fails to explicitly or implicitly exclude polymerization of liposomes. Thus, the phrase set forth above is considered new matter.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 13, 16, 25, 26 and 28-30 remain rejected and newly added claims 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Craig, et al., 1997 (WO 97/28818) in view of Gregoriadis et al., 1999 (Methods, Vol. 19, p. 156-162, IDS), Nagy et al., 2007 (US Patent No. 7,285,289 B2) and Gregoriadis et al., 2006 (US Patent No. 7,008,791 B1, '791) and is repeated for the reasons set forth in the preceding Official action mailed 9-30-08. Applicant's arguments filed 12-30-08 have been fully considered but they are not persuasive.

Applicants argue that Craig does not teach the use of liposomes for the delivery of DNA and protein to cells, and Craig mentions liposomes only when discussing the delivery of DNA or protein to cells. Craig does not specifically suggest the use of liposome to deliver nucleic acids as associated with peptides to cells using liposomes, and the remaining documents fail to suggest associating both nucleic acids and proteins with liposomes (amendment, p. 6-7). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 9-30-08. Craig does teach the use of liposome for the delivery of DNA and protein to cells. Craig teaches administration of a mixture of a nucleic acid encoding a first epitope and a peptide containing a second epitope for vaccinating a mammal against a disease (e.g. abstract). "As used herein, the phrase "means for delivering" a vector to a cell … including viral and non-viral delivery means, by which it is possible to deliver nucleic acid and an antigenic peptide or protein associated with nucleic acid to a mammalian cell, including DNA/polycation complexes, …, microsphere which are used for delivery of DNA or protein to cells, e.g., polylactide glycolide polymers, and liposomes" (e.g. p. 12, 2nd paragraph). Here liposomes can be interpreted as one of the viral and

non-viral delivery means to deliver nucleic acid and an antigenic peptide or protein associated with nucleic acid to a mammalian cell. Even if liposomes are considered an example of microsphere which are used for delivery of DNA or protein, it can be interpreted that the author Craig means although liposome usually is used for delivery of DNA or protein, however, liposome can be used for the delivery of nucleic acid and an antigenic peptide or protein associated with nucleic acid in the present article.

Applicants argue that Nagy reference discusses disadvantages of phospholipid-based liposomes and teaches the use of polymerized liposomes, and Nagy teaches away from displaying a peptide at the surface of a liposome (amendment, p. 7-8).). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 9-30-08. Nagy teaches encapsulating cytokine within a polymerized liposome nanoparticle along with surface display of tumor specific antigen. The arrangement of such surface displayed tumor antigens could easily be optimized for the immune response desired. Nagy may discuss disadvantages of phospholipid-based liposomes but Nagy does NOT teach away from displaying tumor specific antigen on the surface of liposomes. Other cited references Craig, Gregoriadis (1999) and Gregoriadis (2006, '791) all teach using liposomes for delivering DNA and/or peptide or protein to cell. Therefore, it would be obvious to one of ordinary skill in the art at the time of the invention to display an antigenic protein on the surface of a liposome.

Applicants argue that Nagy teaches away from the instant invention because Nagy require nucleic acid to be at the surface of the liposome rather than in the intravesicular space (amendment, p. 8). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 9-30-08. Nagy teaches that the nanoparticle chemistry **allows** proteins,

peptides, carbohydrates and nucleic acids etc., to be attached to the particle surface. Nagy does NOT teach that nucleic acid **has to be** attached to the particle surface. Gregoriadis (2006, '791) teaches preparation of oral vaccines comprising cationic liposomes and, complexed or entrapped within the liposomes, a gene vaccine, that is a nucleic acid encoding for an antigen against which vaccination is desired (e.g. column 1, 1st paragraph). Gregoriadis specifically teach entrapping the gene or nucleic acid within the liposome. Gregoriadis (1999) also teaches entrapment of vaccine, including peptides, protein, and DNA vaccines, in liposomes (e.g. Title, abstract). Therefore, it would be obvious for one of ordinary skill in the art to entrap nucleic acid within the liposome rather than to attached on the surface of the liposome.

Applicants argue that Gregoriadis focus on oral nucleic acid vaccines and the nucleic acid is not required to be in the intravesicular space. The nucleic acid may merely be complexed with the cationic lipids. The practitioner would not be motivated to provide anything other than an oral vaccine. Claims 32 and 33 exclude oral vaccines. Gregoriadis teaches away from combination with Nagy because it teaches not to involve polymerizing the liposome-forming components (amendment, p. 9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 9-30-08. Gregoriadis (1999, 2006) specifically teach entrapping the gene or nucleic acid within the liposome, therefore, it would be obvious for one of ordinary skill in the art to entrap nucleic acid within the liposome. Since the nucleic acid is within a liposome, it would be obvious for one of ordinary skill in the art the nucleic acid is in the intravesicular space, which is within a liposome. Gregoriadis (2006) teaches liposome-entrapped DNA oral vaccine but it does NOT teach that other administration routes are prohibited. In fact, Gregoriadis (1999) also teaches that "[t]he in vivo use of liposomes has been

made by every conceivable route, including the intravenous, intramuscular, subcutaneous, intrahecal, intratracheal, oral, intranasal and topical (skin and a variety of mucosal tissues) routes" (e.g. p. 157, right column to p. 158, left column). Thus, it would be obvious for one of ordinary skill in the art to perform the administration routes as recited in claims 32 and 33. The combination of the references has to viewed as a whole of all of the cited references, the primary reference Craig and those secondary references Gregoriadis (1999), Nagy and Gregoriadis (2006, '791), rather than just Gregoriadis (2006) and Nagy. Nagy may discuss disadvantages of phospholipid-based liposomes but Nagy does NOT teach away from displaying tumor specific antigen on the surface of liposomes. Other cited references Craig, Gregoriadis (1999) and Gregoriadis (2006, '791) all teach using liposomes for delivering DNA and/or peptide or protein to cell. Therefore, it would be obvious to one of ordinary skill in the art at the time of the invention to display an antigenic protein on the surface of a liposome. The teaching of Nagy does not conflict with the teachings of Craig, Gregoriadis (1999) and Gregoriadis (2006). Thus, claims 13, 16, 25, 26 and 28-30 remain rejected and newly added claims 32-35 are rejected under 35 U.S.C. 103(a).

Conclusion

No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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